

We claim:

1. A targeting construct comprising:

(a) a first polynucleotide sequence homologous to an adrenomedullin receptor gene;

(b) a second polynucleotide sequence homologous to the adrenomedullin receptor gene; and

(c) a selectable marker.

2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.

3. A method of producing a targeting construct, the method comprising:

(a) providing a first polynucleotide sequence homologous to an adrenomedullin receptor gene;

(b) providing a second polynucleotide sequence homologous to the adrenomedullin receptor gene;

(c) providing a selectable marker; and

(d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.

4. A method of producing a targeting construct, the method comprising:

(a) providing a polynucleotide comprising a first sequence homologous to a first region of an adrenomedullin receptor gene and a second sequence homologous to a second region of an adrenomedullin receptor gene; and

(b) inserting a positive selection marker between the first and second sequences to form the targeting construct.

5. A cell comprising a disruption in an adrenomedullin receptor gene.

6. The cell of claim 5, wherein the cell is a murine cell.

7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.

8. A non-human transgenic animal comprising a disruption in an adrenomedullin receptor gene.

9. A cell derived from the non-human transgenic animal of claim 8.

10. A method of producing a transgenic mouse comprising a disruption in an adrenomedullin receptor gene, the method comprising:
- (a) introducing the targeting construct of claim 1 into a cell;
  - (b) introducing the cell into a blastocyst;
  - 5 (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
  - (d) breeding the chimeric mouse to produce the transgenic mouse.
11. A method of identifying an agent that modulates the expression of an adrenomedullin receptor, the method comprising:
- 10 (a) providing a non-human transgenic animal comprising a disruption in an adrenomedullin receptor gene;
  - (b) administering an agent to the non-human transgenic animal; and
  - (c) determining whether the expression of adrenomedullin receptor in the non-human transgenic animal is modulated.
- 15 12. A method of identifying an agent that modulates the function of an adrenomedullin receptor, the method comprising:
- (a) providing a non-human transgenic animal comprising a disruption in an adrenomedullin receptor gene;
  - (b) administering an agent to the non-human transgenic animal; and
  - 20 (c) determining whether the function of the disrupted adrenomedullin receptor gene in the non-human transgenic animal is modulated.
13. A method of identifying an agent that modulates the expression of adrenomedullin receptor, the method comprising:
- (a) providing a cell comprising a disruption in an adrenomedullin receptor gene;
  - 25 (b) contacting the cell with an agent; and
  - (c) determining whether expression of the adrenomedullin receptor is modulated.
14. A method of identifying an agent that modulates the function of an adrenomedullin receptor gene, the method comprising:
- (a) providing a cell comprising a disruption in an adrenomedullin receptor gene;
  - 30 (b) contacting the cell with an agent; and

(c) determining whether the function of the adrenomedullin receptor gene is modulated.

15. The method of claim 13 or claim 14, wherein the cell is derived from the non-human transgenic animal of claim 8.

5 16. An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.

17. A transgenic mouse comprising a homozygous disruption in a gene comprising SEQ ID NO:1, or a homolog thereof.

18. The transgenic mouse of claim 17, wherein the transgenic mouse exhibits decreased activity relative to a wild-type control mouse.

10 19. The transgenic mouse of claim 18, wherein the transgenic mouse is hypoactive.

20. The transgenic mouse of claim 18, wherein the decreased activity is characterized by reduced distance traveled in an open field test.

21. The transgenic mouse of claim 18, wherein the decreased activity is characterized by reduced average velocity in the open field test.

15 22. The transgenic mouse of claim 17, wherein the transgenic mouse exhibits increased anxiety relative to a wild-type control mouse.

23. The transgenic mouse of claim 22, wherein the increased anxiety is characterized by reduced percentage of time spent in the central region of an open field test.

20 24. Phenotypic data associated with the transgenic mouse of claim 17, wherein the phenotypic data is in a database